CORRESPONDENCE

Platelet Transfusion in Hematology, Oncology and Surgery

by Prof. Dr. med. Hannes Wandt, Dr. med. Kerstin Schäfer-Eckart, Prof. Dr. med. Andreas Greinacher in issue 48/2014

Platelet Transfusion and Hemorrhage

Recently, two prospective randomized multicenter studies on hypoproliferative thrombocytopenia compared prophylactic transfusion of platelet concentrates below a threshold of 10 000/µL with therapeutic platelet transfusions only, administered at onset of hemorrhages other than mucocutaneous bleeding (1, 2). In the patient group with only therapeutic platelet transfusion, a significant increase in the incidence of grade 2, 3 or 4 (World Health Organization [WHO] bleeding scale) hemorrhages was observed. This applied to both patients with acute myeloid leukemia (AML) and patients after autologous stem cell transplantation. However, since the most severe form of hemorrhage—intracerebral hemorrhage—occurred only in AML patients, Wandt et al. (1) regarded the available evidence as being sufficient to adopt a therapeutic-only platelet transfusion strategy in adult, clinically stable patients after autologous stem cell transplantation.

However, this strategy requires monitoring at close intervals for signs of hemorrhage which can be realized during clinical studies, but not in a standard hospital setting. In addition, the immediate availability of platelet concentrates in the event of hemorrhage cannot be guaranteed at all times, even in tertiary care hospitals. Moreover, platelet concentrates with reduced platelet content and pathogen-inactivated platelet concentrates are commercially available in German-speaking countries. Prospective studies evaluating these types of platelet concentrates observed sporadic cases of intracranial hemorrhage even when platelet transfusions are applied prophylactically. To pursue a therapeutic-only platelet transfusion strategy using these types of platelet concentrates would expose patients to unpredictable risks.

In the best interest of the safety of patients suffering from hypoproliferative thrombocytopenia, we firmly reject the position of Wandt et al. (3) and agree with Professor Slichter from Seattle who wrote in a 2013 editorial of the Ị ew England Journal of Medicine (4), 'In my opinion, the reduction in the use of platelet transfusions does not justify subjecting patients to the increased bleeding risks associated with a therapeutic-only platelet-transfusion strategy in any category of patients with hypoproliferative thrombocytopenia'.

DOI: 10.3238/arztebl.2015.0505a

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Exemption: Promyelocytic Leukemia

Wandt et al. have rightly pointed out that in many clinically stable patients with hematologic malignancies, the transfusion trigger can be set at <10 000/µL (1).

However, there is the exemption of promyelocytic leukemia. As the result of hyperfibrinolysis, the degradation of coagulation factors by proteolytic enzymes from the leukemia cells, and of cytokines, patients with this type of leukemia can develop disseminated intravascular coagulation (DIC) and ultimately a rapidly life-threatening coagulopathy (2).

According to German and international guidelines, platelet counts should be maintained at 30 000–50 000/µL in these patients (3, 4). Replacement treatment should be started very early, at times even before the diagnosis has been confirmed by molecular genetic testing (2).

DOI: 10.3238/arztebl.2015.0505b

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In Reply:

Both letters highlight the fact that the risk for hemorrhage varies between patients with thrombocytopenia. However, even doubling the standard dose of platelets in a prophylactic transfusion strategy cannot prevent clinically relevant hemorrhages, as it has been shown recently in a large study with more than 1000 patients (1). The same study also confirmed that the risk for hemorrhage varies widely between different patient populations. This risk was particularly low in patients after autologous stem cell transplantation. Today's quality guidelines already provide different recommendations for each type of patients according to their risk for hemorrhage. The aim for the future is to further improve our ability to more clearly define risk groups (for example, patients with acute leukemia during induction chemotherapy) and identify low-risk patients (for example, patients after autologous stem cell transplantation) so that we can establish specific platelet transfusion regimes. The small population of patients with promyelocytic leukemia is, for example, at a very high risk for hemorrhage prior to achieving remission and at that time requires a particularly intensive treatment with platelet transfusions in combination with coagulation-modifying agents. We would like to thank J. Mezger for pointing this out in his letter. Likewise, the platelet counts of patients with prolonged episodes of hypoproliferative thrombocytopenia after intensive chemotherapy should be checked at least once or twice daily, as it was required in the prospective studies. However, contrary to the statement in R. Zimmermann's letter, these studies did not require "monitoring at close intervals". Hospitals where this minimum standard is not ensured and where adequate platelet transfusions cannot be provided within 4 hours after diagnosis of a hemorrhage (this was the timeframe required in those studies, not "immediate" transfusion) should not treat leukemia patients or perform hematopoietic stem cell transplantations at all. This applies regardless of the transfusion strategy used as it would involve unpredictable risks, not only with regard to hemorrhage.

Applying a therapeutic transfusion strategy to treat patients after autologous hematopoietic stem cell transplantation does not increase the risk for severe hemorrhage and reduces platelet transfusions by one third—this is confirmed by published data and recent experiences with several hundred patients. The likelihood of minor hemorrhage is slightly higher for the therapeutic transfusion strategy as it implies that platelet transfusion are only started once the patient has already developed a minor bleeding.

Transfusion specialists and experienced hematologists agree with this differentiated approach (2, 3). Platelet transfusion are not only beneficial, but allogenic, biological treatments that should only be administered after careful benefit-risk evaluation (4).

Further analysis of the available data (5) and additional clinical studies are needed to establish a differentiated platelet transfusion therapy that can be used in the future to improve the lives of our patients.

DOI: 10.3238/arztebl.2015.0506

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Conflict of interest statement
The authors of all contributions declare that no conflict of interest exists.